Optimal flow rate for antegrade cerebral perfusion

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Objective: Antegrade cerebral perfusion is widely used in neonatal heart surgery, yet commonly used flow rates have never been standardized. The objective of this study was to determine the antegrade cerebral perfusion flow rate that most closely matches standard cardiopulmonary bypass conditions.

Methods: Nine neonatal piglets underwent deep hypothermic cardiopulmonary bypass at a total body flow of 100 mL/kg/min (baseline). Antegrade cerebral perfusion was conducted via innominate artery cannulation at perfusion rates of 10, 30, and 50 mL/kg/min in random order. Cerebral blood flow was measured using fluorescent microspheres. Regional oxygen saturation and cerebral oxygen extraction were monitored.

Results: Cerebral blood flow was as follows: baseline, 60 ± 17 mL/100 g/min; antegrade cerebral perfusion at 50 mL/kg/min, 56 ± 17 mL/100 g/min; antegrade cerebral perfusion at 30 mL/kg/min, 36 ± 9 mL/100 g/min; and antegrade cerebral perfusion at 10 mL/kg/min, 13 ± 6 mL/100 g/min. At an antegrade cerebral perfusion rate of 50 mL/kg/min, cerebral blood flow matched baseline ($P = .87$), as did regional oxygen saturation ($P = .13$). Antegrade cerebral perfusion at 30 mL/kg/min provided approximately 60% of baseline cerebral blood flow ($P < .002$); however, regional oxygen saturation was equal to baseline ($P = .93$). Antegrade cerebral perfusion at 10 mL/kg/min provided 20% of baseline cerebral blood flow ($P < .001$) and a lower regional oxygen saturation than baseline ($P = .011$). Cerebral oxygen extraction at antegrade cerebral perfusion rates of 30 and 50 mL/kg/min was equal to baseline ($P = .53, .48$) but greater than baseline ($P < .0001$) at an antegrade cerebral perfusion rate of 10 mL/kg/min. The distributions of cerebral blood flow and regional oxygen saturation were equal in each brain hemisphere at all antegrade cerebral perfusion rates.

Conclusion: Cerebral blood flow increased with antegrade cerebral perfusion rate. At an antegrade cerebral perfusion rate of 50 mL/kg/min, cerebral blood flow was equal to baseline, but regional oxygen saturation and cerebral oxygen extraction trends suggested more oxygenation than baseline. An antegrade cerebral perfusion rate of 30 mL/kg/min provided only 60% of baseline cerebral blood flow, but cerebral oxygen extraction and regional oxygen saturation were equal to baseline. An antegrade cerebral perfusion rate that closely matches standard cardiopulmonary bypass conditions is between 30 and 50 mL/kg/min. (J Thorac Cardiovasc Surg 2010;139:530-5)

Antegrade cerebral perfusion (ACP) was developed as an alternative to deep hypothermic circulatory arrest (DHCA) as a cardiopulmonary bypass (CPB) management strategy for complex arch reconstructions. The question of whether ACP is less morbid than DHCA is controversial. Although this issue will not be addressed in this study, it remains a fact that ACP is widely used in the clinical setting. There are no data documenting how much flow the brain receives during ACP or how ACP brain flow compares with brain flow during many standard CPB conditions. This study addresses the question of how much blood flow is needed during ACP to provide the level of oxygen delivery to the brain that is equivalent to that delivered using total-body CPB. Our premise for the study is that because ACP is a widely used bypass strategy for complex arch reconstructions, it is important to understand how ACP flow rates relate to actual cerebral oxygen delivery.

ACP has evolved over the past 15 years. However, the perceived ideal ACP flow rate varies 3-fold among different centers (20–63 mL/kg/min)[1-4] and has never been standardized. During neonatal deep hypothermic (18°C–20°C) CPB, a total body flow rate of 100 mL/kg/min is commonly used in practice as a standard.[5] The ACP rate that provides cerebral perfusion equal to the standard total body flow rate of 100 mL/kg/min has not been determined.

During ACP, the innominate artery is cannulated, and thus, direct perfusion is isolated to the right cerebral hemisphere and right arm, whereas the left cerebral hemisphere is perfused via the Circle of Willis. The left and right regional blood flow distribution in the brain during ACP is not well documented.

We determined cerebral blood flow (CBF) at a total body flow rate of 100 mL/kg/min and at each of 3 different ACP rates under deep hypothermic CPB to determine their relation. Regional blood distribution in the brain (right and

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Abbreviations and Acronyms

ACP = antegrade cerebral perfusion
CBF = cerebral blood flow
CPB = cardiopulmonary bypass
DHCA = deep hypothermic circulatory arrest
NIRS = near-infrared spectroscopy
rSO2 = regional oxygen saturation

left hemispheres) and cerebral oxygen metabolism were also investigated.

MATERIALS AND METHODS

All animals received humane care in compliance with the *Guide for the Care and Use of Laboratory Animals* (www.nap.edu/catalog/5140.html). Neonatal piglets (n = 9), weighing 3.5 to 4.4 kg, underwent induction of anesthesia with intramuscular ketamine (10 mg/kg) and atropine (0.04 mg/kg), and were intubated with a 3-mm cuffed endotracheal tube. Animals were ventilated to normocapnia on 100% oxygen. Anesthesia was maintained with inhalation of 1% to 2% isoflurane. In addition, fentanyl 5 μg/kg was administered before CPB, and muscle relaxation was provided with 0.1 mg/kg doses of pancuronium bromide. Rectal and nasopharyngeal temperatures were continuously monitored.

Pressure monitoring catheters were placed in the right femoral artery and right subclavian artery, and a central venous line was placed under direct vision through an incision in the left jugular vein.

Cardiopulmonary Bypass Circuit and Experimental Protocol

The animals were placed supine, a midline sternotomy was performed, the heart and great vessels were exposed, and heparin (300 IU/kg) was administered. The innominate artery was cannulated (6F or 8F arterial BioMedicus; Medtronic, Minneapolis, Minn), a 14F single-stage venous cannula (Edwards Lifesciences, Irvine, Calif) was inserted into the right atrial appendage, and CPB was initiated.

The CPB circuit consisted of a roller pump (COBE Cardiovascular Inc, Arvada, Colo), a membrane oxygenator (Dideco Kids D100, Sorin Group USA, Arvada, Colo), an arterial filter (Dideco Kids D130, Sorin Group USA), and quarter-inch inside diameter tubing. The circuit was primed with donor pig blood mixed with crystalloid prime solution (Normosol R; Abbott Laboratories, North Chicago, Ill) to maintain hematocrit no less than 30%. In addition, heparin 1000 IU and sodium bicarbonate (5 mEq) were added to the priming solution.

CPB was initiated with the aid of vacuum-assisted venous drainage. Additional fentanyl (10 μg/kg) was administered to the piglet, and 1% to 2% isoflurane was continued on the pump. Core cooling was commenced at a pump flow of 200 mL/kg/min using pH-stat arterial blood gas management, and hematocrit was maintained between 25% and 30%. Phentolamine was administered during the cooling process at 0.2 mg/kg to facilitate an even and effective cooling process that was conducted for a minimum of 30 minutes to ensure uniform cooling of the central nervous system. Continuous blood gas monitoring during cooling was performed with Terumo CDI (Terumo CDI 500; Terumo Corporation, Tokyo, Japan). Inflow temperature was meticulously controlled and kept no lower than 10°C below the measured nasopharyngeal temperature. Once nasopharyngeal temperature reached 18°C, total body perfusion rate was reduced to 100 mL/kg/min for 15 minutes, the aorta was clamped, and cold cardioplegia (Plegisol; Abbott Laboratories) was administered via the aortic root. CBF was then measured at a total body flow of 100 mL/kg/min using 15-μm microspheres injected into the pump outflow line, and the value obtained under this standard CPB condition was chosen as the reference baseline CBF for comparison with ACP.

The proximal innominate artery, left carotid artery, and left subclavian artery were clamped, and ACP was initiated at each of 3 perfusion rates (10, 30, or 50 mL/kg/min) in random order. Each perfusion rate was continued for 15 minutes before switching to the next flow rate, and microspheres were injected at each rate to determine CBF. The piglets were then euthanized, the brains were dissected, and microsphere-derived CBF was determined as milliliters of blood flow/100 g tissue/min. CBF at each of the ACP rates was then compared with the baseline CBF at total body perfusion (100 mL/kg/min). Bihemispheric regional cranial oxygen saturations[6] (rSO2) were continuously monitored using bilateral cranial near-infrared spectroscopy (NIRS) sensors (INVOS model 5100C cerebral oximeter with SPFP pediatric sensors; Somantics Corporation, Troy, MI) during the procedure. Blood samples from the right subclavian artery and left jugular vein were simultaneously withdrawn to calculate cerebral oxygen extraction at baseline and under each ACP condition.

Microsphere Assay

All microsphere procedures were performed with reference to the classic review by Heymann[7] and protocols from the Fluorescent Microsphere Resource Center (University of Washington, Division of Pulmonary and Critical Care Medicine, Seattle, Wash; http://fmrc.pulmcc.washington.edu/Documents.shtml). In each experiment, 4 different colors of 15-μm diameter polystyrene microspheres (FluoSpheres; Molecular Probes, Eugene, Ore) were used for the injections. Each color of microsphere was supplied as an aqueous suspension at a concentration of 1.0×10^6 microspheres per milliliter. Before use, the microspheres were resuspended by sonication; 0.2 mL of the suspension (200,000 beads) was withdrawn from the stock vial, added directly into 6 mL of blood from the bypass circuit, mixed gently by several inversions, and then injected into the pump outflow line.

After euthanization, the brain was removed and hemispheres were divided at the middle. Each hemisphere was subdivided to cortex, medulla (hippocampus and brain stem), and cerebellar subregions.

The tissue subregions were further dissected into smaller portions as needed, weighed and transferred to 50 mL polyethylene tubes, and digested in 4 mol/L ethanolic potassium hydroxide (224.4 g potassium hydroxide per liter of 100% ethanol) containing a final concentration of 0.5% Tween 80 at a maximum ratio of 5 g of tissue per 40 mL solvent. To calculate recovery rate during the microsphere extraction procedure, 4000 microspheres (200 μL of a 20,000 sphere/mL suspension in 0.25% Tween 80) of an additional color microsphere was added to each weighed tissue aliquot as an internal standard. Recovery rate was calculated from each sample, ranging from 79% ± 12% to 91% ± 11%, with a grand mean calculated as 85% ± 19% recovery (n = 322 determinations, including other studies conducted in our laboratory). The 85% recovery value was used to correct the measured concentration of microspheres in each sample.

To enhance digestion, the tubes were placed in a 50°C water bath for 48 hours and manually shaken after 24 hours. The digested samples were centrifuged (30 minutes at 2000*g*), and the supernatant was carefully removed. The pellet, containing microspheres and some debris, was completely resuspended in 1% Triton X-100 by vortexing and then centrifuged again (30 minutes at 2000*g*). A final rinsing step was performed with phosphate buffer (0.01 mol/L, pH 7.4). After the final centrifugation, the supernatant was carefully removed while preventing disturbance of the pellet. Finally, 3 mL of 2-ethoxyethyl acetate was added to the pellet to extract the fluorescent dye from the microspheres. Tubes were then vortexed and allowed to stand for approximately 24 hours, vortexed again, and centrifuged (30 minutes at 2000*g*), leaving a clear solvent in which fluorescence was determined.

Fluorescence was determined with a SpectraMax M5e plate reader (Molecular Devices, Sunnyvale, Calif) with an excitation wavelength range

from 350 to 636 nm and an emission wavelength range from 428 to 680 nm. The concentration of microspheres (microspheres/milliliter of solvent) was calculated from standard curves generated from serial dilutions of known concentrations of each color microsphere dissolved in 2-ethoxyethyl acetate.

Cerebral Blood Flow and Cerebral Perfusion Pressure

Injected microspheres are distributed to body tissues in proportion to the blood flow to each tissue and trapped in the capillary bed. Thus, the distribution fraction is calculated as follows: distribution fraction = microspheres in the tissue/total microspheres injected.

If the cardiac output is known, a quantitative measure of blood flow (Q_{Tissue}, mL/min) can be obtained: Q_{Tissue} = cardiac output × distribution fraction.

Cardiac output can be considered equal to pump flow rate during CPB, and CBF was calculated with the following formula: CBF (mL/100 g/min) = pump flow rate × microsphere counts in the brain/200,000.

Cerebral perfusion pressure was calculated as (mean subclavian arterial pressure – jugular venous pressure).

Cerebral Metabolism

Right subclavian arterial and left jugular venous blood samples were obtained simultaneously for calculation of cerebral oxygen extraction (arteriovenous oxygen content difference): % cerebral oxygen extraction = (CaO2 – CvO2)/CaO2 × 100, where CaO2 was the arterial oxygen content and CvO2 was the venous oxygen content.

Arterial and venous blood pH, oxygen tension, carbon dioxide tension, hematocrit, and oxygen saturation, as well as glucose and lactate, were measured with using an ABL 825 analyzer (Radiometer America, Westlake, OH).

Statistical Analysis

Data are given as mean ± standard deviation. Statistical analysis was performed with JMP statistical software version 6 (JMP USA, SAS Inc, Cary, NC). Blood flow values in brain tissue were first compared among brain subregions (cortex, medulla, and cerebellum) at each flow rate. Next, the flow data were aggregated by summation into right and left hemisphere flows and compared as right and left hemisphere flows, which were found to be statistically equal. The reported CBF is therefore a global value representing the sum of flow values for a total of 6 subregions (3/hemisphere). CBF, rSO2, and cerebral extraction of oxygen at different ACP flow rates were compared using 1-way analysis of variance for multiple comparisons followed by Dunnett's post hoc test. Right and left side blood flow and rSO2 were compared using paired *t* test corrected for multiple comparisons.

RESULTS

Blood Flow to the Brain

CBF was found to change with ACP rate (Figure 1). CBF rates at ACP-10 (13 ± 6 mL/100/min, $P < .001$, n = 9) and ACP-30 (36 ± 9 mL/100 g/min, $P < .002$, n = 9) were lower than that of baseline (60 ± 17 mL/kg/min, n = 8). CBF at an ACP rate of 50 mL/kg/min matched the CBF achieved during baseline (56 ± 17 mL/100 g/min, $P = .87$, n = 9). The rate of increase in CBF was linearly dependent on ACP flow rate ($y = 1.076x + 2.427$, $R^2 = 0.7221$, $P < .001$, n = 27) (Figure 2, *A*) and cerebral perfusion pressure ($y = 0.671x + 2.502$, $R^2 = 0.6353$, $P < .001$, n = 27) (Figure 2, *B*). CBF as percent of cardiac output was also determined (Figure 2, *C*). At baseline, fractional flow to the brain was 6.5% ± 1.8% (n = 8). During ACP, fractional flow to the brain was approximately 2 times that of baseline at all ACP flow rates (ACP-10, 14% ± 6%, $P = .006$, n = 9; ACP-30, 13% ± 3%, $P = .02$, n = 9; ACP-50, 13% ± 5%; $P = .01$, n = 9).

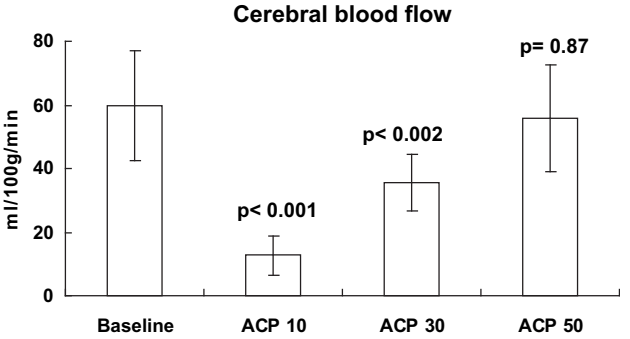

FIGURE 1. CBF during ACP. CBF at baseline (total body flow of 100 mL/kg/min) and each ACP flow rate was measured. CBF at ACP rate of 10 and 30 mL/kg/min was lower than that of baseline ($P < .001$, $P < .002$, n = 9, 9 vs baseline of 60 ± 17, n = 8). CBF at an ACP rate of 50 mL/kg/min (56 ± 17 mL/100g/min, $P = .87$, n = 9) matched the CBF achieved during baseline. *ACP,* Antegrade cerebral perfusion.

Cerebral Oxygen Extraction

We computed cerebral oxygen extraction at baseline and different ACP flow rates (Figure 3). Percent oxygen extraction by the brain was approximately 3 times higher at an ACP rate of 10 mL/kg/min than that of baseline (37 ± 14 vs 13 ± 8, n = 8, 8; $P < .0001$). However, at an ACP rate of 30 or 50 mL/kg/min, it was not different from baseline (18 ± 9, $P = .53$, n = 9; 8 ± 3, $P = .48$, n = 9), although there was a trend for cerebral oxygen extraction to be lower at ACP-50.

Regional Oxygen Saturation

rSO2 determined by NIRS was measured for each blood flow rate. The average rSO2 of the right and left hemispheres was computed for each flow rate in each experiment, and these mean cerebral rSO2 values were used for statistical analyses (Figure 4). Compared with baseline (79 ± 13, n = 8), rSO2 was lower at an ACP rate of 10 mL/kg/min (62 ± 15, $P = .011$, n = 8) and equal at ACP rates of 30 mL/kg/min (82 ± 9, $P = .93$, n = 9) and 50 mL/kg/min (90 ± 4, $P = .13$, n = 9).

Distribution of Blood Flow and Oxygen to Right and Left Cerebral Hemispheres

We compared the distribution of blood flow and oxygen delivery between right and left brain hemispheres. At baseline total body flow and each of the ACP flow rates, the blood flow rates to the left and right hemispheres were equal (Figure 5, *A*: baseline, $P = .75$; ACP-10, $P = .67$; ACP-30,

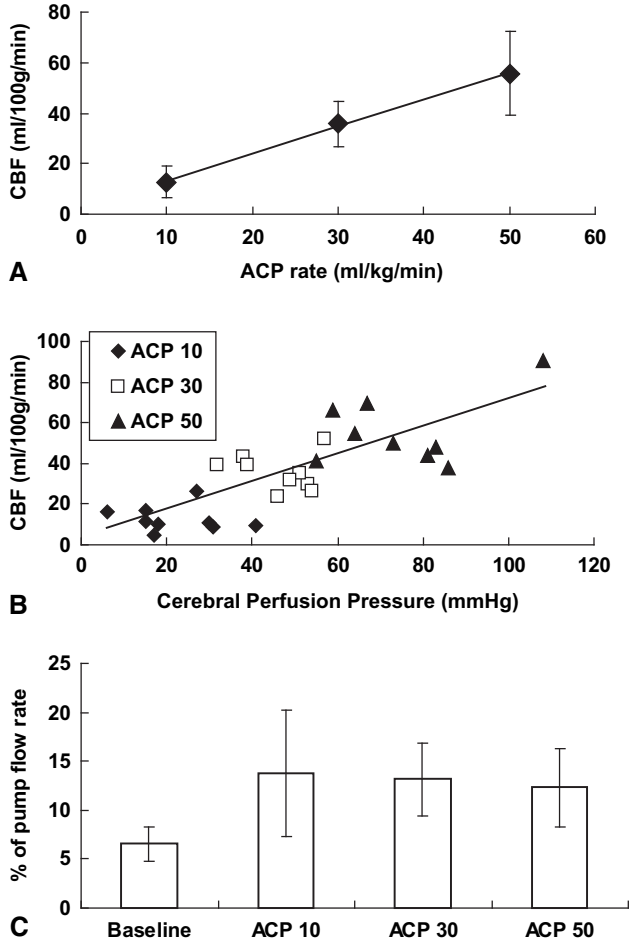

FIGURE 2. A, Relation between CBF and ACP flow rates. The rate of increase in CBF was linearly dependent on ACP flow rate ($y = 1.076x + 2.427$, $R^2 = 0.7221$, $P < .001$, $n = 27$). B, Relation between CBF and perfusion pressure. The rate of increase in CBF was linearly dependent on cerebral perfusion pressure ($y = 0.671x + 2.502$, $R^2 = 0.6353$, $P < .001$, $n = 27$). C, CBF as percent of cardiac output. CBF was calculated as fraction of pump flow under different flow conditions. At baseline, fractional flow to the brain was 6.5% ± 1.8% ($n = 8$). During ACP, fractional flow to the brain was approximately 2 times that of baseline at all ACP flow rates (ACP-10, 14% ± 6%, $P = .006$, $n = 9$; ACP-30, 13% ± 3%, $P = .02$, $n = 9$; ACP-50, 13% ± 5%; $P = .01$, $n = 9$). *ACP,* Antegrade cerebral perfusion; *CBF,* cerebral blood flow.

$P = .60$; and ACP-50, $P = .96$). Similarly, there were no differences between left and right cerebral hemisphere rSO2 values at any of the measured flow rates (Figure 5, *B*: baseline, $P = .85$; ACP-10, $P = .36$; ACP-30, $P = .64$; ACP-50, $P = .63$).

DISCUSSION

The purpose of the present study was to determine the optimal ACP flow rate under deep hypothermic CPB. We compared the CBF at 3 different ACP rates with that at a standard CPB total body flow rate of 100 mL/kg/min.

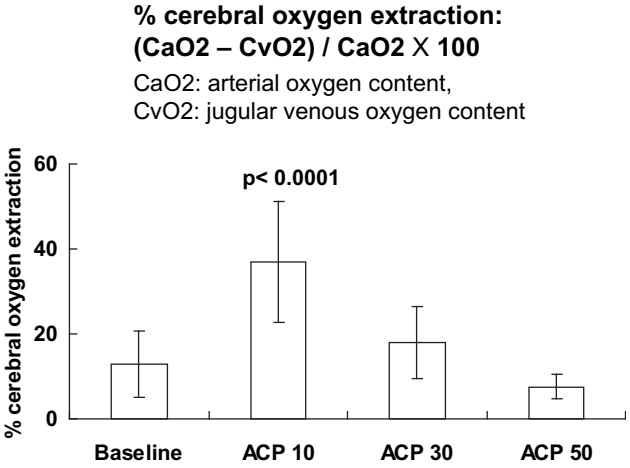

FIGURE 3. Cerebral oxygen extraction during ACP. Cerebral oxygen extraction was approximately 3 times higher at an ACP rate of 10 mL/kg/min than that of baseline (37 ± 14% $P < .0001$, $n = 8$, vs baseline 13 ± 8, $n = 8$). However, at an ACP rate of 30 or 50 mL/kg/min, it was not different from baseline (18 ± 9%, $P = .53$, $n = 9$; 8 ± 3%, $P = .48$, $n = 9$). *ACP,* Antegrade cerebral perfusion.

We chose the 100 mL/kg/min standard CPB condition as the baseline because it is a flow rate that is uniformly accepted as meeting metabolic demand during CPB at 18°C. We fully acknowledge that opinions may differ on this value, because some consider lower flows as safe at these temperatures. This baseline was selected as a reference point for the study and understanding of ACP. Our data showed that CBF increased with ACP rate. CBF at an ACP rate of

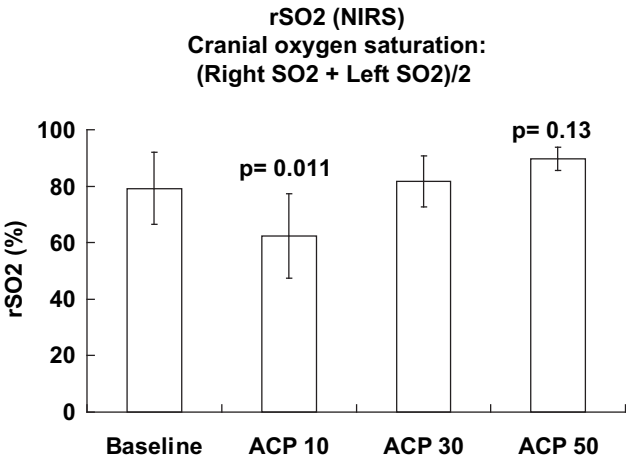

FIGURE 4. Cranial oxygen saturation during ACP. Blood distribution between right and left hemispheres was evaluated by NIRS. The average cerebral oxygen saturation of right and left hemispheres was calculated, and baseline total body flow (79% ± 13%, $n = 8$) was compared with rSO2 under ACP conditions. It was lower at an ACP rate of 10 mL/kg/min (62 ± 15, $P < .011$, $n = 8$) but equal to baseline at ACP rates of 30 mL/kg/min (82 ± 9, $P = .93$, $n = 9$) and 50 mL/kg/min ($P = .13$, $n = 9$). *rSO2,* Regional oxygen saturation; *NIRS,* near-infrared spectroscopy; *ACP,* antegrade cerebral perfusion.

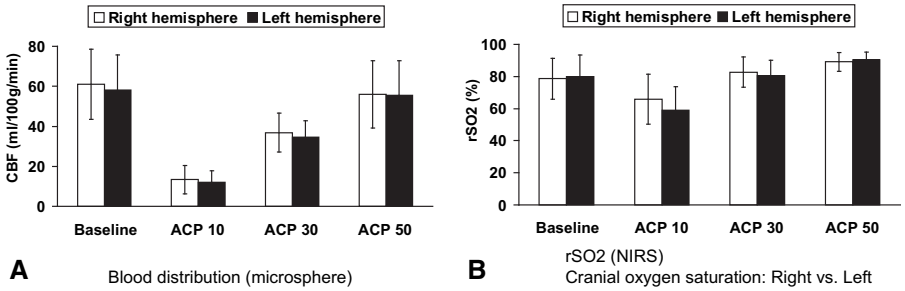

FIGURE 5. Comparison of blood flow and oxygen distribution to right and left brain hemispheres. CBF distribution to left and right brain hemispheres was measured during baseline total body flow and ACP at 3 flow rates. There was no difference in CBF to left and right sides of the brain during baseline total body flow or any of the ACP flow rates (A, baseline, $P = .75$; ACP-10, $P = .67$; ACP-30, $P = .60$, and ACP-50, $P = .96$). We also compared rSO2 in right and left cerebral hemispheres at different blood flow rates. We found that there were no differences between left and right cerebral hemisphere rSO2 values at baseline total body flow or any of the ACP flow rates (B, baseline, $P = .85$; ACP-10, $P = .36$; ACP-30, $P = .64$; ACP-50 $P = .63$). *CBF,* Cerebral blood flow; *ACP,* antegrade cerebral perfusion; *rSO2,* regional oxygen saturation; *NIRS,* near-infrared spectroscopy.

50 mL/kg/min was equal to CBF at baseline total body flow, and CBF at an ACP rate of 30 mL/kg/min was approximately 60% of baseline CBF. However, rSO2 and cerebral oxygen extraction data revealed that an ACP rate of 30 mL/kg/min could provide sufficient oxygen compared with baseline. Under deep hypothermia (18°C), cerebral vascular autoregulation is not present.[8] In our experiments, CBF increased linearly with ACP rate and cerebral perfusion pressure, confirming that autoregulation is not operative during ACP at these temperatures (Figure 2).

The anatomy of neck and intracranial vessels in pigs is different from that of humans. In pigs, the innominate artery gives rise to both carotid arteries and to the right subclavian artery. Despite these anatomic differences, in our pig model, the direction of blood flow (right to left) during ACP was similar to that of humans. In our experiments, we cannulated and perfused the innominate artery and clamped the left carotid artery and the left subclavian artery to initiate ACP. Isolated CBF was provided by the right carotid artery and right vertebral artery (by way of the right subclavian artery). The left cerebral hemisphere is perfused via the Circle of Willis, as in humans.

Distribution of systemic blood flow during CPB was reported in 1973.[9] In this study, microspheres were injected into monkeys at a flow rate of 200 to 250 mL/kg/min under normothermia. The mean percentage of total systemic blood flow to the brain was approximately 10%. Another group[10] reported the blood distribution under normal conditions. The distribution to the brain was 11% of cardiac output in human adults, 2.6% in dogs, and 4% in newborn lambs. Our study showed that fractional flow to the brain was 6.5% under conditions of CPB at total body flow rate of 100 mL/kg/min at 18°C, a value well within the range expected from previously reported findings. Under all 3 ACP flow rates studied, fractional flow to the brain was approximately 13% of pump output (Figure 2, *C*). This increase in percentage of pump flow rate to the brain is to be expected because we are isolating flow to the upper body only during ACP. From another perspective, however, the observation that only 13% of flow goes to the brain during ACP presents many opportunities to investigate and understand the destination of the majority of the pump flow (87%) during ACP.

Measurement of rSO2 by NIRS has played an important role in the elucidation of the impact of congenital heart surgery on cerebral hemodynamics.[11] Measurement of rSO2 using NIRS devices indicates regional oxygen metabolism and the balance of local tissue oxygen supply versus demand. Daubeney and colleagues[12] reported a close correlation between cerebral regional oxyhemoglobin saturation measured by NIRS and jugular bulb saturation ($r = 0.69$, $P < .0001$) in 40 children undergoing cardiac catheterization or cardiac surgery. Our data also revealed that cerebral oxygen extraction was inversely proportional to the NIRS values and that CBF was directly related to rSO2.

CONCLUSIONS

CBF increases with ACP flow at 18°C, and there are no left/right hemisphere imbalances even under very low ACP flows. Compared with our chosen baseline flow of 100 mL/kg/min under conditions of standard CPB, an ACP rate of 30 mL/kg/min provides approximately 60% of baseline CBF, but rSO2 and cerebral oxygen extraction are equal to the baseline data, suggesting equal oxygenation in the brain. On the other hand, an ACP rate of 50 mL/kg/min provides CBF equal to baseline, but rSO2 trended higher than baseline and cerebral oxygen extraction trended lower than baseline, suggesting more oxygenation in the brain. This suggests that higher ACP rates in the ''clinically acceptable'' range may provide excessive blood flow to the brain and potentially have a deleterious effect, including endothelial damage. DeCampli and colleagues[13] reported that regional low-flow perfusion at a higher flow rate was associated with upper torso edema, greater post-CPB acidosis, and an overall declining clinical course after CPB. Further studies should focus on these concerns. In addition, some surgeons are now using ACP at temperatures of 25°C or

28°C, a condition under which the brain oxygen demand also increases. A higher ACP flow rate may be needed to provide sufficient blood flow to the brain at higher ACP temperatures. An understanding of the flow characteristics of ACP methodology under moderate and mild hypothermia, including the influence of vascular autoregulation, is needed.

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Discussion

Dr Randall Griepp *(New York, NY)*. I have no financial disclosures. Dr Sasaki, I congratulate you and your colleagues on addressing the issue of optimizing perfusion during pediatric cardiac surgery. I have a number of comments, criticisms, and questions, but I do have a soft spot for my colleagues from my former alma mater, so I will be as tactful as possible.

In optimizing perfusion, what we are really looking at is cerebral protection and survival of the animals with normal neurologic function. Why not develop a survival model, wake the animals up and make sure that you haven't injured them?

Dr Sasaki. In this study our main focus was comparing blood flow under conditions of ACP with that under standard CPB. The relationship between the 2 bypass techniques has never been established. We didn't choose a survival model for this study, but in the future we plan to do so to investigate cerebral histology after ACP.

Dr Griepp. The cerebral metabolic rate for oxygen is affected by the pH of the perfusate and whether you use selective cerebral perfusion or CPB. Why not cannulate the sagittal sinus so you can get a reasonable estimate of mixed venous saturation from the brain, and then you can calculate CMR02 and determine whether CMR02 is changing under the circumstances of your experiment?

Dr Sasaki. We agree that we may see more accurate values from sagittal sinus sampling. But in our piglet models we use very small animals (3–4 kg), so the available area is very small and there is limited space for multiple monitoring devices. We were primarily interested in bilateral NIRS monitoring for this study, so we didn't collect the samples from the sagittal sinus. Instead, we collected venous samples from the left jugular vein and calculated oxygen metabolism.

Dr Griepp. Okay, but it's troubling to hear pediatric surgeons say that the blood vessels are too small to work with. The final question has to do with the issue of autoregulation and pH of the perfusion. There is reasonably good experimental evidence that use of pH-stat when cooling animals in preparation for hypothermic circulatory arrest improves cooling, and there's some clinical evidence to suggest that pH-stat under those circumstances is preferable. However, under the circumstances of continuous selective cerebral perfusion, I do not believe there is any experimental evidence, or any clinical evidence, that pH-stat is preferable. We have shown in a similar model that pH-stat and alpha-stat differ profoundly, and the pH-stat clearly destroys autoregulation at these temperatures. The excessive cerebral flow increases intracranial pressure and cerebral metabolic rate for oxygen and undoubtedly increases the potential for microemboli because the flow is much greater than that needed for oxygen delivery. Why use pH-stat continuous selective cerebral perfusion? Why not use alpha-stat under these circumstances?

Dr Sasaki. We followed our institutional protocol, which precluded survival for these studies. Our surgeons use pH-stat during cooling, so we'd like to reproduce the clinical situation as much as possible in the piglet model. As you mentioned, it's still a controversial problem regarding optimal blood gas management during selective cerebral perfusion, so I think I also need to do another kind of experiment focusing on optimal blood gas management in the next step. In this study, we manipulated a number of variables and anticipate exploring alpha-stat in the future.

Dr Griepp. Once again, I congratulate you and your colleagues for approaching these important but difficult questions.